

# FDA Goals for the Committee on Evidence-Based Opioids Prescribing for Acute Pain

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# Misuse and Abuse of Rx Opioids Remains an Important Public Health Problem

- In 2017, prescription opioids were the largest category of pharmaceutical products misused and abused in US
  - 11.1 million people estimated to have past-year misuse/abuse
  - 1.7 million people estimated with DSM IV criteria for substance use disorder involving prescription opioid analgesics
- In comparison, 886,000 estimated to have past-year heroin use

**Source:** Substance Abuse and Mental Health Services Administration. (2018). Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSDUH Series H-53). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from <https://www.samhsa.gov/data/>.

# Consequences: Prescription Opioids and Overdose Death in the US



## Drugs Involved in U.S. Overdose Deaths, 1999 to 2017

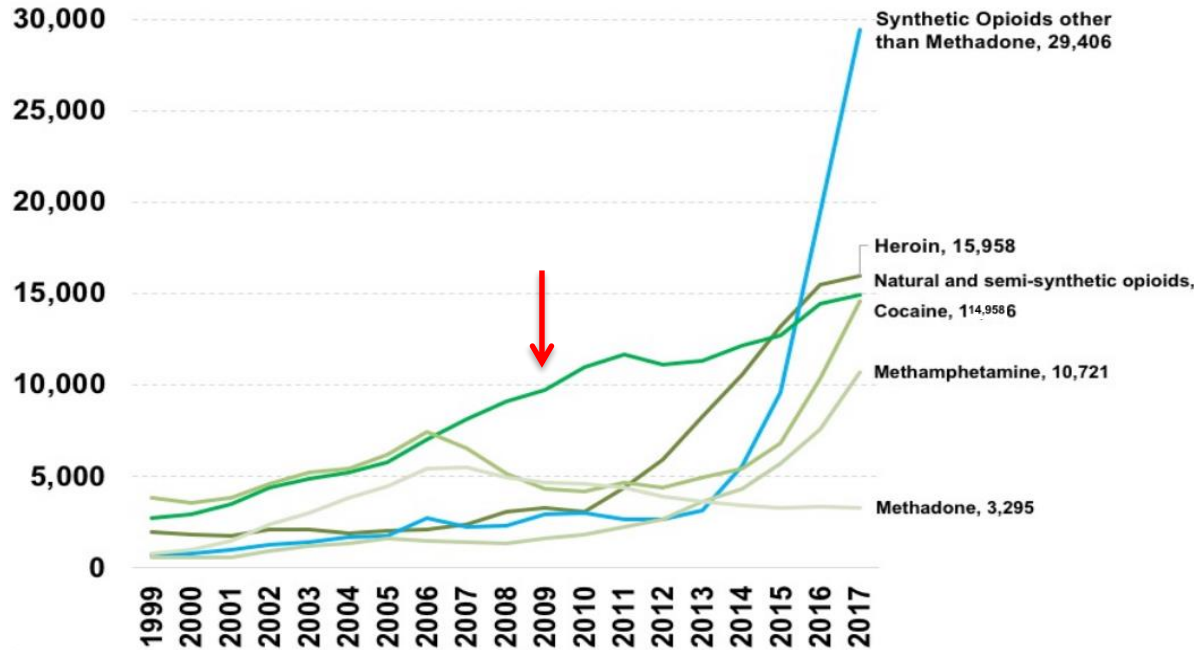
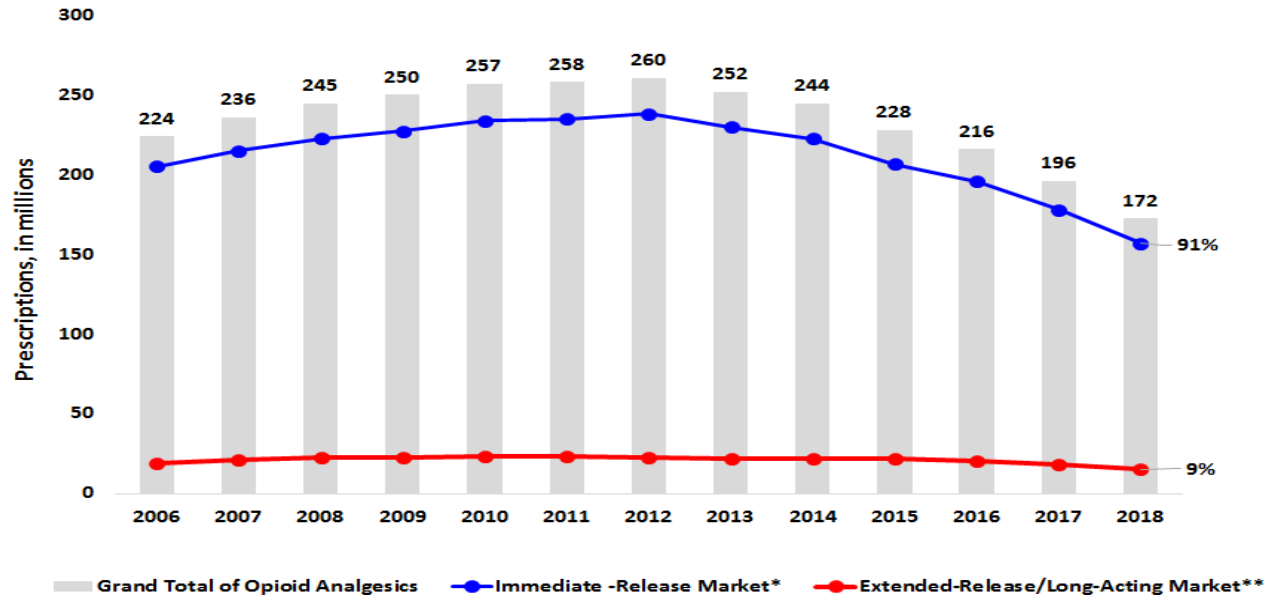


Figure Source: National Institute on Drug Abuse Data Source: CDC Wonder  
Available from: <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>

# Crisis Ongoing Despite Falling # of Prescriptions for Opioid Analgesics



\*Immediate-Release formulations include oral solids, oral liquids, rectal, nasal, and transmucosal

\*\*Extended-Release/Long-Acting formulations include oral solids and transdermal patches

Note: Include opioid analgesics only, excluding injectable formulations as well as opioid-containing cough-cold products and opioid-containing medication-assisted treatment (MAT) products

# The FDA and Opioid Abuse/Misuse

"Unquestionably, our greatest immediate challenge is the problem of opioid abuse. This is a public health crisis of staggering human and economic proportion ... we have an important role to play in reducing the rate of new abuse and in giving healthcare providers the tools to reduce exposure to opioids to only clearly appropriate patients, so we can also help reduce the new cases of addiction."

- Scott Gottlieb, FDA Commissioner  
Address to FDA staff, May 15, 2017

# The Opioid Crisis: FDA's Priorities

1. Decreasing Exposure & Prevent New Addiction

2. Supporting the Treatment of Those With Opioid Use Disorder

3. Fostering the Development of Novel Pain Treatment Therapies

4. Improving Enforcement & Assessing Benefit-Risk

# The Opioid Crisis: FDA's Priorities & Strategies

## 1. Decreasing Exposure & Prevent New Addiction



**Appropriate Dose/Duration Labeling**



**Appropriate Packaging, Storage, and Disposal**



**Health Care Provider Education**

## 2. Supporting the Treatment of Those With Opioid Use Disorder



**Naloxone**



**Medication Assisted Treatment (MAT)**

## 3. Fostering the Development of Novel Pain Treatment Therapies



**Partnerships & Meetings**



**Abuse Deterrent Formulations (ADFs)**



**Pain Treatment Alternatives**

## 4. Improving Enforcement & Assessing Benefit-Risk



**Improving Enforcement**



**Assessing Benefit-Risk**

# Improved Opioid Prescribing: Priorities Align with Recently Passed SUPPORT Act

- Substance Use-Disorder Prevention that Promotes Opioid Recovery and Treatment (SUPPORT)
- Many new provisions affecting FDA including tools to:
  - **Reduce exposure to opioids as a way to lower the rate of new addiction**
  - Require certain packaging, such as unit dose blister packs, for opioids and other drugs that pose a risk of abuse or overdose
  - Require that opioids be dispensed with a mail-back pouch or other safe disposal option
  - Stop illegal, illicit, unapproved, counterfeit and potentially dangerous drugs more efficiently from entering the U.S. through the IMFs



# The Need to Improve Opioid Prescribing

- Excess numbers of opioids being prescribed for acute pain
- Potential consequences of excess opioids

# Opioid Analgesic Needs Vary by Condition/Procedure--Unused Opioids Common

Procedure	Mean/ (range) tablets filled	Mean/Median tablets used	~Days Used	~Leftover tablets
Outpatient Shoulder Surgery	60 (n.d.)*	37*	9-10	23
Cesarean Delivery	40 (5-80)*	20*	4-5	20
Tooth Extraction	28 (n.d.)	13	2-3	15
Upper Extremity Surgery	30 (n.d.)	14 (Bone); 9 (Soft Tissue)	2-3	15
Laparoscopic Cholecystectomy	30 (0-100)	10-12	2-3	20
Laparoscopic Appendectomy	30 (n.d.)*	12*	2-3	18
Partial Mastectomy with Node Biopsy	23 (0-60)	6	1-2	17
Laparoscopic Inguinal Hernia Repair	33 (15-70)	9	1-2	24
Open Inguinal Hernia Repair	30 (15-120)	9	1-2	21
Partial Mastectomy	21 (0-50)	3	1	18
Dermatologic Surgery	9 (3-20)	4	1	5

1. Hill, et al., *Ann Surg*, 2017

2. Bateman, et al., *Obstet Gyn*, 2017

3. Maughan, et al., *Drug Alc Dep*, 2016

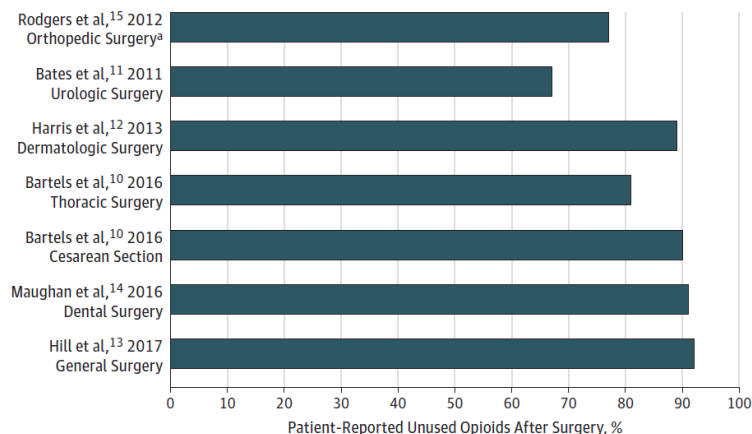
4. Harris, et al., *JAMA Dermatol*, 2013

5. Bockman, et al., *J Pain*, 2017 (Abstract)

6. Kumar, et al., *AJSM*, 2017

# Leftover Opioid Analgesics Reported in Post-surgical Populations

Figure. Prevalence of Unused Opioids Prescribed After Surgery

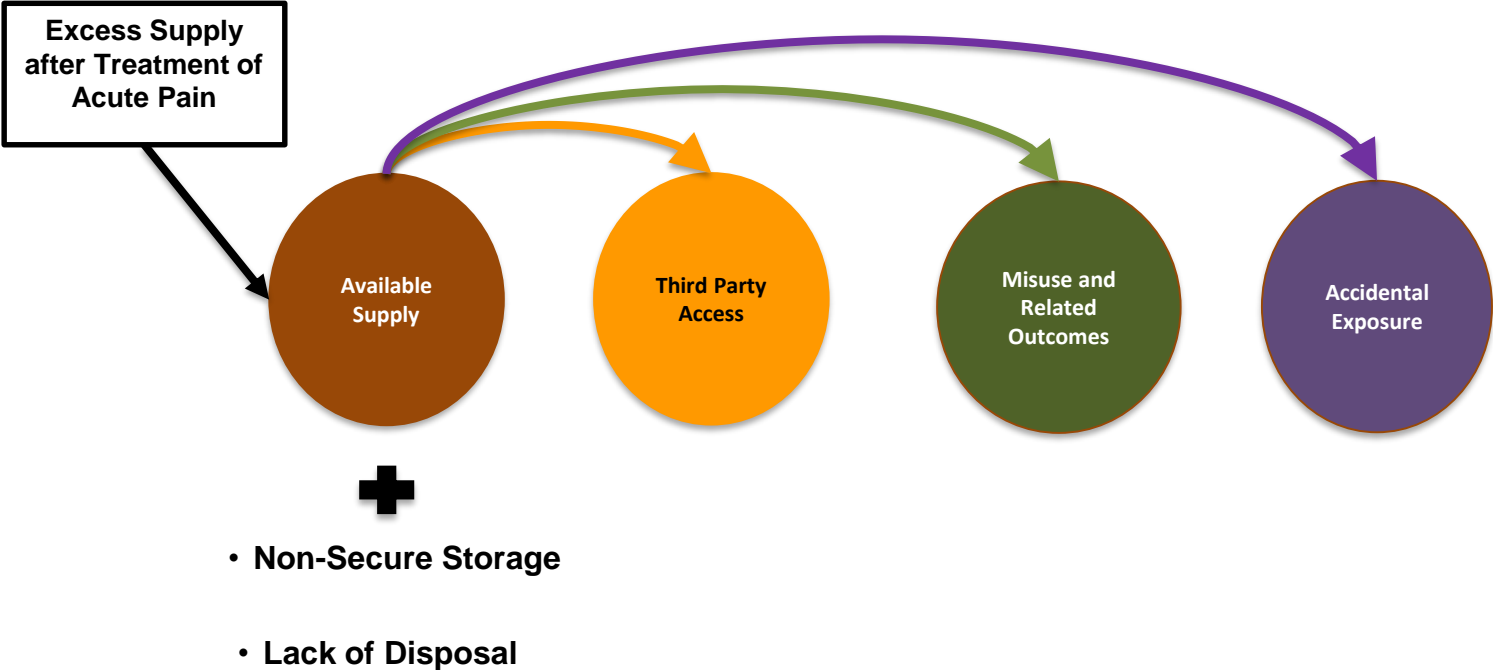


<sup>a</sup>percentage of patients reporting use of 15 tablets or fewer

**Figure Source:** Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review. JAMA Surg. 2017 Nov 1;152(11):1066-1071.

- **Across many surgical procedures,**
  - **>50% of patients reported excess supply of opioid analgesics after treatment of acute pain**
  - **Many patients kept excess supply and stored supply in unsecured locations**

# Opioid Analgesics in the Home Can Feed Other Problems



# FDA Response: Support Rational Opioid Prescribing

- Continue work to provide educational tools to prescribers through Continuing Medical Education
- Explore packaging solutions
  - Utility of a defined, short-term supply of medication packaged in a manner that limits the number of pills dispensed
  - Utility of packaging that could make it easier to track the number of doses that have been taken or reduce the risk for third-party access, such as teens ingesting pills they found in a medicine cabinet
- **Support the development of objective, evidence-based guidelines for use of opioids in acute pain**

# Rational Prescribing for the Condition/Procedure

- “[FDA is] also taking new steps to encourage medical professional societies to develop evidence-based guidelines on appropriate prescribing of opioids for different medical indications. The FDA will be working with these important stakeholders to help advance the development of these new, evidence-based prescribing recommendations.”<sup>1</sup>
- FDA has contracted with National Academies of Sciences, Engineering, and Medicine to develop evidence-based guidelines for opioid analgesics for acute pain **specific to conditions or procedures**<sup>2</sup>

1. FDA Statement by FDA Commissioner Scott Gottlieb, M.D., on balancing access to appropriate treatment for patients with chronic and end-of-life pain with need to take steps to stem misuse and abuse of opioids. July 9, 2018. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm612779.htm>

2. FDA Statement August 22, 2018: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm617908.htm>

# Tasks for the Committee

- Identify the best available evidence for prescribers and provide a framework for its evaluation
- Support more appropriate prescribing of opioids while ensuring that patients with pain are adequately treated
- Support development of new evidence where needed for clear, rigorous, evidence-based guidelines

# Statement of Work: Framework Development

- Develop a framework for evaluating the evidence base underpinning clinical treatment guidelines for opioid prescribing for acute pain
  - Develop a threshold level of evidence needed to support such guidelines
- Consider standards established in the 2011 IOM Report *Clinical Practice Guidelines We Can Trust* and other established standards for clinical assessment



# Statement of Work: Assess Current State of Data on Prescribing

- Inventory surgical and medical conditions associated with acute pain where opioids are used
  - Assess available information on dose and duration of opioid use by indication, including existing opioid prescribing guidelines for acute pain conditions
  - Apply evidence framework
- Identify and prioritize acute pain conditions where rigorous evidence is needed to inform prescribing guidelines

# Sources of Data

**Focus is on data quality and applicability  
not on the source**

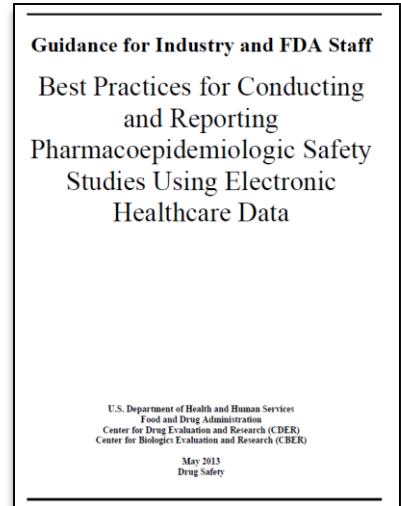
# Evaluating Data Quality/Study Methods

## Data Quality

- Procedures to ensure completeness, consistency, and accuracy of data collection and management;
- Frequency and type of error corrections or changes in data adjudication policies during the relevant period of data collection;
- Changes in key data elements during the study time frame and any potential effect on the study; and
- Report on missing data over time

## Study Methods

- Study design, including comparator groups;
- Study population and time period of study, including:
  - Study time frame and scheduled milestones
  - Data sources used;
  - Drug exposures of interest;
  - Drug safety outcomes of interest;
  - Methods to control for sources of bias and confounding



# Statement of Work: Research Agenda

- Develop a prioritized research agenda for
  - Work to develop new treatment-specific treatment guidelines
  - Work to support additional rigorous evidence to expand on existing guidelines
  - Agenda should include a minimum of 5 conditions for indications that are abuse-prone and/or commonly prescribed

# Summary

- FDA goal is to improve the state of the science supporting clinical practice guidelines for acute pain
  - Creating a framework for evidence generation and assessment
  - Inventorying existing treatment of acute pain and available evidence on opioid use
  - Creating a research agenda for prioritizing future work
- This framework can then be used to improve the prescribing of opioids while ensuring that patients with acute pain are adequately treated

# **FDA is Seeking NASEM Help to Support Rational Opioid Prescribing for Acute Pain**

**Be evidence-driven**

**If the evidence doesn't exist, work to get it**

# Thank You





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